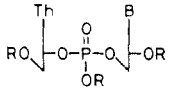
recommend the procedures of Table II using allyloxycarbonyl chloride (AOCCl) (**22**)[7] or allyl 1-benzotriazoylcarbonate (AOCOBT) (**23**),[8] where choice of the base and solvent is important for obtaining satisfactory yields.

The AOC group is also employable for the sugar-hydroxyl protection.[4,9] The *O*-allyloxycarbonylated nucleoside **8** was prepared in 95% yield by *tert*-butylmagnesium chloride (2 equiv) aided reaction of cytidine nucleoside **13** (1 equiv) and the AOC agent **22** (1.2 equiv). When this *O*-AOC nucleoside was treated with a catalytic amount of $Pd[P(C_6H_5)_3]_4$ in the presence of HCOOH/n-$C_4H_9NH_2$ (2 equiv each) for 1 h, **13** was brought back. Conveniently, the Pd(0)-catalyzed reaction of the N,O-bis(allyloxycarbonylated) derivative **5** removed contemporaneously both protections to afford the nucleoside **7** in quantitative yield.

Internucleotide linkage is protectable by allyl group.[10] The above described characteristic properties of AOC, coupled with the phosphite method using allyl phosphorodichloridite, enabled us to open an extremely convenient way to dinucleoside phosphates. The key operation here is complete deprotection of fully-protected dinucleoside phosphotriester intermediates by single treatment with Pd(0) catalyst. Thus, collidine-assisted (4.6 equiv) condensation of the 3′-O-unprotected thymidine nucleoside **21** (2 equiv), $CH_2{=}CHCH_2OPCl_2$ (2 equiv), and the 5′-O-free adenosine **6** (1 equiv) followed by NO_2 oxidation (THF, −78 °C) afforded the protected TpA **24** in 80% yield. When **24** was treated with a mixture of $Pd[P(C_6H_5)_3]_4$ and $P(C_6H_5)_3$ (5 and 20 mol %/allyl), formic acid (10 equiv), and butylamine (10 equiv) in THF at room temperature for 30 min, the four allylic protecting groups were removed all at once from the nucleoside base, sugar hydroxyl, and internucleotide bond to give TpA (**25**) in 97% yield.



24, B = Ad^{AOC}; R = AOC

25, B = Ad; R = H

In summary, the AOC group acts as both specific and general protectors. This method is useful in view of mildness of the deprotection conditions and simplicity of the workup, providing a powerful tool in nucleotide synthesis.

Supplementary Material Available: Experimental details (16 pages). Ordering information is given on any current masthead page.

(7) We are grateful to Hodogaya Chemicals, Co., for the generous gift of allyloxycarbonyl chloride.

(8) AOCOBT (**23**), mp 107–111 °C, was prepared by the triethylamine-promoted (1 equiv) reaction of AOCCl (**22**) (1 equiv) and 1-hydroxybenzotriazole (1 equiv) in THF at room temperature for 10 min.

(9) Guibe, F.; M'Leux, Y. S. *Tetrahedron Lett.* **1981**, *22*, 3591.

(10) Hayakawa, Y.; Uchiyama, M.; Kato, H.; Noyori, R. *Tetrahedron Lett.* **1985**, *26*, 6505.

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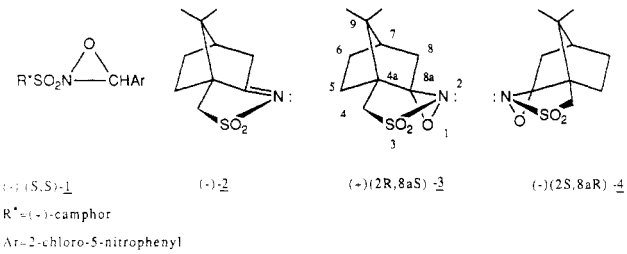
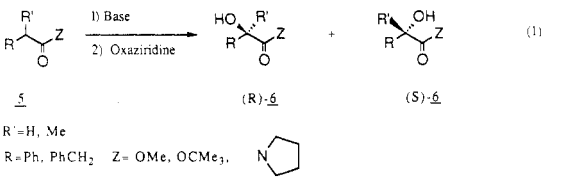
Asymmetric Oxidation of Ester and Amide Enolates Using New (Camphorylsulfonyl)oxaziridines

Summary: The first asymmetric oxidation of ester and amide lithium enolates **5** to optically active α-hydroxy carbonyl compounds **6** is reported using new, easily prepared, stable (camphorylsulfonyl)oxaziridines (+)-(2*R*,8a*S*)-**3** and (−)-(2*S*,8a*R*)-**4**. Either enantiomer of **6** can be readily obtained because the configuration of the oxaziridine three-membered ring determines the product stereochemistry.

Sir: Optically active α-hydroxy carbonyl compounds are versatile chiral building blocks for asymmetric synthesis and are important structural subunits of natural products.[1] Recently we[2] and Evans[3] independently reported that oxidation of chiral enolates, using 2-(phenylsulfonyl)-3-phenyloxaziridine (**1**, R* = Ar = Ph), is an attractive route to these valuable compounds in high optical purity (80–98% de).[4] However, a disadvantage of any chiral auxiliary based asymmetric synthesis is the necessity of preparing and eventually removing the chiral auxiliary reagent.

We now report the first examples of a simple procedure for the synthesis of *both* enantiomers of α-hydroxy compounds **6** in good optical purity. This procedure involves the asymmetric oxidation of enolates using new, readily available camphorsulfonic acid derived sulfonyloxaziridines (+)-**3** and (−)-**4** (eq 1).





Our previous studies have demonstrated that chiral 2-sulfonyloxaziridines, such as (−)-(*S*,*S*)-**1**, are useful asymmetric oxidizing reagents which give high enantioselectivities for the oxidation of certain unfunctionalized sulfides and alkenes.[5-8] However, in the synthesis of

(1) For leading references on chiral α-hydroxy carbonyl compounds, see: (a) Brown, H. C.; Pai, G. G.; Jadhav, P. K. *J. Am. Chem. Soc.* **1984**, *106*, 1531. (b) Gamboni, R.; Mohr, P.; Waespe-Sarcebvic, N; Tamm, C. *Tetrahedron Lett.* **1985**, 203. (c) Oppolzer, W.; Dudfield, P. *Helv. Chim. Acta* **1985**, *68*, 216.

(2) Davis, F. A.; Vishwakarma, L. C. *Tetrahedron Lett.* **1985**, 3539.

(3) Evans, D. A.; Morrissey, M. M.; Dorow, R. L. *J. Am. Chem. Soc.* **1985**, *107*, 4346.

(4) The MoOPH oxidation of ester enolates using a camphor-based chiral auxiliary has been reported (14–93% de).[1b]

(5) For a review of the asymmetric oxidations using chiral 2-sulfonyloxaziridines, see: Davis, F. A.; Jenkins, R. H., Jr. In *Asymmetric Synthesis*; Morrison, J. D.; Ed.; Academic: New York, 1984, Vol. 4, Chapter 4, pp 313–353.

(6) Asymmetric oxidation of sulfides: (a) Davis, F. A.; Lamendola, J. F., Jr.; Nadir, U.; Kluger, E. W.; Sedergran, T. C.; Panunto, T. W.; Billmers, R.; Jenkins, R., Jr.; Turchi, I. J.; Watson, W. H.; Chen, J. S.; Kimura, M. *J. Am. Chem. Soc.* **1980**, *102*, 2000. (b) Davis, F. A.; McCauley, J. P., Jr.; Harakal, M. E. *J. Org. Chem.* **1984**, *49*, 1466.

0022-3263/86/1951-2402$01.50/0

Table I. Asymmetric Oxidation of Lithium Enolates Using Chiral Sulfonyloxaziridines 1, 3, and 4 at −78 °C in THF

				RR′C(OH)C(O)Z (6)		
entry	oxaziridine	RR′CHC(O)Z (5), R, R′, Z	conditions	% ee	absolute config	yield,[a] %
1	(+)-(2*R*,8a*S*)-3	Ph, H, OMe		54.0	(−)-*R*[b]	84
2			HMPA[c]	12.0	(−)-*R*	88
3	(+)-(2*R*,8a*S*)-3	Ph, H, $OCMe_3$		64.4	(−)-*R*[b]	82
4			−90 °C	71.0	(−)-*R*	84
5	(−)-(2*S*,8a*R*)-4		−90 °C	66.4	(+)-*S*	86
6			HMPA[c]	34.5	(−)-*R*	82
7	(+)-(2*R*,8a*S*)-3	$PhCH_2$, H, OMe	−90 °C	58.0	(+)-*R*[d]	73
8			HMPA,[c] −90 °C	85.5	(+)-*R*	63
9	(−)-(*S*,*S*)-1	Ph, H, NC_4H_8		41.0	(+)-*S*[e]	71
10	(+)-(2*R*,8a*S*)-3			30.0	(+)-*S*	70
11			−90 °C	18.0	(+)-*S*	85
12			HMPA[c]	50.0	(−)-*R*	74
13	(−)-(2*S*,8a*R*)-4			21.0	(−)-*R*	73
15	(−)-(*S*,*S*)-1	Ph, Me, NC_4H_8[f]		40.0	(−)-*R*	60
16	(+)-(2*R*,8a*S*)-3			60.0	(−)-*R*[e]	77
17			−90 °C	46.0	(−)-*R*	70
18			HMPA[c]	20.0	(+)-*S*	35
19	(−)-(2*S*,8a*R*)-4		0 °C	36.4	(+)-*S*	54

[a] Isolated yield of pure material (>98%). [b] Based on the maximum reported rotations reported in ref 1a. [c] Ratio of THF/HMPA, 20:1. [d] Reference 19. [e] % ee determined by using a Daicel Chiral Pak OT (+) HPLC column, 25 cm × 0.46 cm; solvent, MeOH; flow rate, 0.5 mL/min. First to be eluted was (−)-(*R*)-6 (R = Ph, R′ = H, Z = NC_4H_8), (−)-(*R*)-6 (R = Ph, R′ = Me, Z = NC_4H_8).[19] [f] The lithium enolate was generated at 0 °C (30 min) before cooling to −78 °C for oxidation.

(+)-kjellmanianone (−)-*1* gave low chemical yields and only moderate stereoselectivities (up to 36.5% ee).[9]

While chiral 2-sulfonyloxaziridines are readily prepared by oxidation of the sulfonimines (R*SO_2N=CHAr) separation of the resulting oxaziridine diastereoisomers is necessary.[6] Significantly, biphasic oxidation of **2**, using potassium peroxymonosulfate (Dupont Oxone)/18-crown-6 for 5 days in benzene, affords a single (camphorylsulfonyl)oxaziridine isomer, (+)-(2*R*,8a*S*)-**3**, in 94% isolated yield.[10,14] The oxaziridine three-membered ring has the 2*R*,8a*S* configuration because oxidation is possible only from the exo face of the C=N double bond in **2**.[6a,15] Oxidation of the *l*-10-camphorsulfonic acid derived isomer of **2**[6a] gave the (−)-(2*S*,8a*R*)-4 (93%) isomer.[10]

Summarized in Table I are results of the asymmetric oxidation of the lithium enolates of some representative esters and amides **5** by oxaziridines **1**, **3**, and **4** (eq 1). It is known that enolate geometry has a significant influence on enantiofacial selectivity.[16] Consequently these compounds were chosen because their lithium enolates are well defined.[17] Typically, enolates were preformed by addition of a THF (5–6 mL) solution of **5** (0.25 mmol) to 1.5 equiv of lithium diisopropylamide (LDA) in 5–6 mL of THF at −78 °C. After 25–30 min, 2.0 equiv of **1**, **3**, or **4**, dissolved in 5 mL of THF, was added and the reaction mixture quenched after 15 min with saturated NH_4Cl solution. Products were isolated by preparative TLC (silica gel) eluting with 20% ether–pentane for the esters and 50% ether–pentane for the amides. Enantiomeric purities and absolute configurations of **6** were established by comparison with authentic samples and the use of a chiral HPLC column (Table I).[19]

The results summarized in Talbe I illustrate that asymmetric oxidation of enolates using oxaziridines **3** and **4** affords α-hydroxy carbonyl compounds **6** with good enantioselectivity and in good to excellent chemical yield (eq 1). Lower enantioselectivities were observed for oxaziridine (−)-(*S*,*S*)-**1**. In all previous studies of asymmetric oxidations by chiral sulfonyloxaziridines the product stereochemistry is determined by the configuration of the oxaziridine three-membered ring with nonbonded steric interactions responsible for the chiral recognition.[5,6] The stereochemistry of α-hydroxycarbonyl compounds **6** are also determined by the geometry of the oxaziridine three-membered ring with (+)-(2*R*,8a*S*)-**3** and (−)-(2*S*,8a*R*)-**4** giving opposite configurations of **6** (Table I).

(7) Asymmetric oxidation of selenides: Davis, F. A.; Stringer, O. D.; McCauley, J. M., Jr. *Tetrahedron* **1985** *41*, 4747.

(8) Asymmetric epoxidation: Davis, F. A.; Harakal, M. E.; Awad, S. B. *J. Am. Chem. Soc.* **1983**, *105*, 3123.

(9) Boschelli, D.; Smith, A. B., III; Stringer, O. D.; Jenkins, R. H., Jr.; Davis, F. A. *Tetrahedron Lett.* **1981**, 4385.

(10) Oxidation of **2**[6a] (5.0 g, 23.0 mmol) was carried out according to the procedure of Curci et al.[11] except that the reaction was allowed to go for 5 days at a pH 8.0, using a $NaHCO_3$ buffer. (+)-**3** and (−)-**4** were purified by flash chromatography (silica gel) using CH_2Cl_2 as the eluent. (+)-**3** (94% yield): mp 165–167 °C; $[\alpha]_D$ +44.59° (*c* 2.19, $CHCl_3$). (−)-**4** (93% yield): mp 163–165 °C; $[\alpha]_D$ −43.59° (*c* 2.16, $CHCl_3$).[13] A more detailed description of these oxaziridines will appear elsewhere.[12]

(11) Curci, R.; Fiorentino, M.; Troisi, L.; Edwards, J. O.; Pater, R. H. *J. Org. Chem.* **1980**, *45*, 4758.

(12) Davis, F. A.; Towson, J. C., submitted for publication.

(13) Satisfactory analysis were obtained for all new compounds, and their spectral properties were consistent with their structures.

(14) The IUPAC and CA name for compound **3** is: (2*R*,4a*S*,7*R*,8a*S*)-tetrahydro-9,9-dimethyl-4*H*-4a,7-methanooxazirino[3,2-*i*][2,1]benzisothiazole 3,3-dioxide.

(15) (a) Pirkle, W. H.; Rinaldi, P. L. *J. Org. Chem.* **1978**, *43*, 4475. (b) Forni, A.; Moretti, I.; Torre, G.; Vignudelli, E. *Tetrahedron Lett.* **1979**, 907.

(16) For excellent discussions of enolate geometry and their effects on asymmetric induction, see: (a) Evans, D. A. In *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic: Orlando, 1984; Vol. 3, pp 1–100. (b) Heathcock, C. H. In *Asymmetric Synthesis*; Morrison, J. d., Ed.; Academic: Orlando, 1984; Vol. 3, pp 111–206.

(17) The lithium enolate of methyl phenyl acetate **5** (R = Ph, R′ = H, Z = OMe is reported to exist as a 71:29 mixture of the *Z*/*E* enolates which imporved to 95/5 in the presence of HMPA.[18] The lithium enolate of methyl-3-phenyl propionate is assumed to be predominantly the (*E*) enolate in the absence of HPMA but has the *Z* enolate in the presence of HMPA.[18] Enolates derived from *N*-pyrrolidine amides are reported to have the *Z* geometry in the absence or presence of HMPA.[1,16a]

(18) Ireland, R. E.; Muller, R. H; Willard, A. K. *J. Am. Chem. Soc.* **1976**, *98*, 2868.

(19) Optically pure **6** (R = $PhCH_2$, R′ = H, Z = OMe) was prepared by refluxing optically pure (−)-(*S*)-hydroxy-3-phenylpropanoic acid with methanol/5-Å molecular sieves/TsOH catalyst for 2 days; $[\alpha]_D$ −7.6° (*c* 2.0 $CHCl_3$). The pyrrolidine group in (−)-(*R*)-**6** (R′ = H), mp 92 °C (41.2% ee), $[\alpha]_D$ −26.2° (*c* 1.5 $CHCl_3$), was removed as previously described[2] by refluxing with 10 mL of 2 M H_2SO_4 for 4 h to give after isolation, by preparative TLC, (−)-(*R*)-mandelic acid (70%) 40% ee. Attempts to hydrolyze (acid or base) atrolactic acidic amide **6** (R = Ph, R′ = Me) without racemization has been unsuccessful to date. The configuration of this compound was tentatively assigned by comparison of its order of HPLC elution from the chiral column and its sign of rotation, mp 104–106 °C (58% ee), $[\alpha]_D$ −41.8° (*c* 2.2, absolute EtOH), to amide (−)-(*R*)-**6** (R = Ph, R′ = H).

The asymmetric oxidation of amide enolates appears to be different than the ester enolates. For example, (+)-(2*S*,8a*R*)-**3** gave (*R*)-**6** with ester enolates, but (*S*)-**6** with amide **5** (R′ = H) and (*R*)-**6** with amide **5** (R′ = Me) (Table I, compare entries 1, 3, and 7 with 10 and 15). Note also that a lower temperature (−90 °C) resulted in lower enantioselectivities for the amides but higher enantioselectivities for the esters.

We believe that the origins of the enantioselection are a consequence of steric and metal chelation effects. In part, the preliminary results in Table I can be rationalized by attack of the lithium enolate on the oxaziridine oxygen atom from the sterically least hindered direction, assuming that "OLi" is the sterically more demanding group.[20] Asymmetric oxidations of enolates in the presence of HMPA suggest that metal chelation also has some role in defining the transition-state geometry.[21] HMPA is generally thought to disrupt metal chelation and oxidations under these conditions should be more sensitive to steric effects.[16] For the ester enolates, the presence of HMPA results in lower enantioselectivities (compare entries 1 and 2, 3 and 6). However, ester **5** (R = $PhCH_2$, R′ = H, Z = OMe), which should be the least sterically demanding, on oxidation with (+)-**3** gave (+)-(*R*)-**6** in 58% and 85.5% ee, respectively, in the absence and presence of HMPA (entries 7 and 8). Asymmetric oxidation of the bulky pyrrolidine amide enolates in the presence and absence of HMPA results in a change in the steroselection (compare entries 10 and 15 with 12 and 17).

It seems likely that the results summerized in Table I can be explained in terms of steric and metal chelating effects which reinforce and in some cases oppose one another. However, steric factors seem to predominate. At this time a more precise transition-state hypothesis is not possible because of a lack of knowledge of metal chelating effects involving sulfonyloxaziridines and enolates.

In summary, the first synthesis of a readily available, stable asymmetric oxidizing reagent, (camphorylsulfonyl)oxaziridines **3** and **4**, is described. These reagents afford useful levels of enantioselection for the asymmetric oxidation of ester and amide enolates to α-hydroxy carbonyl compounds **6**. Experiments are under way to further define the mechanism and scope of asymmetric enolate oxidations using chiral sulfonyloxaziridines.

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(21) Possible sites of metal chelation in the oxaziridine are the sulfonyl oxygens[22] and the electron pair on the oxaziridine nitrogen atom. [15a]

(22) For examples of metal chelation involving sulfonyl oxygens, see: Trost, B. M.; Schmuff, N. R., *J. Org. Chem.* **1985**, *50*, 396. Hellwinkel, D.; Lenz, R.; Lammerzahl, F. *Tetrahedron* **1983**, *39*, 2073. Oppolzer, W.; Chapuis, C.; Bernardinelli, G. *Helv. Chim. Acta* **1984**, *67*, 1397.